Amendments to the Specification:

Please delete the previously filed Sequence Listing and insert therefor the substitute Sequence Listing filed herewith.

Please replace paragraph [0025] with the following amended paragraph:

[0025] Thin layer chromatography and liquid chromatography/mass spectrometric analyses, as well as Repetitive Extragenic Palindrome Polymerase Chain Reaction (REP-PCR), indicate considerable strain to strain chemical and genetic diversity. Bioassay-guided fractionation of one active extract has led to the isolation of a novel series of metabolites that includes a potent cytotoxin (IC_{50} = 10 ng/ml against the HCT-116 human colon carcinoma cell line) that has been named salinosporamide A ~~(Figure 2)~~ (Figure 1). This molecule is most closely related to clasto-lactacystin beta-lactone (also called omuralide), the intermediary hydrolysis product of lactacystin, an anti- microbial product. Salinosporamide A represents the first natural product to be discovered that possesses a fused beta-lactone gamma-lactam bicyclic ring and is a highly potent anticancer agent.

Please replace paragraph [0026] with the following amended paragraph:

[0026] The Salinospora group was initially recognized after phylogenetic characterization of sediment-derived actinomycetes isolated during an expedition to the Bahamas. Partial 16S rDNA gene sequences from eight morphologically diverse strains indicated the presence of four signature nucleotides between positions 207-468 *(E. coli* numbering system; Table 3). These signatures have subsequently been found in all 45 partially sequenced Salinospora strains. Two strains showing the highest phylogenetic diversity (CNH643 and CNH646) were sequenced nearly in their entirety (GenBank accession numbers AY040619 (SEQ ID NO:3) and AY040620 (SEQ ID NO:4), respectively) and found to possess one additional signature nucleotide (position 1456) that is also characteristic of this group (Table 3). Phylogenetic analyses of aligned sequences from these strains indicate that they form a distinct and coherent clade within the Micromonosporaceae ~~(Figure 3)~~ (Figure 2). Signature nucleotides unify this

clade and a high bootstrap value supports clear separation from the nine currently described genera within the family.

Please replace paragraph [0028] with the following amended paragraph:

[0028] A follow-up study was undertaken in the Bahamas to determine the persistence of the *Salinospora* group. From *20* samples collected from four transects (0-30 m), 355 actinomycetes were observed and over 90% of these displayed characteristic *Salinospora* morphologies suggesting that this group may be the numerically dominant actinomycete in marine sediments. Of those observed, 100 strains were isolated for further study. The average numbers of *Salinospora* colony-forming units (cfu's) ranged from 1.2-2.3 x 10^3 cfu's/ml sediment. Over 50% of the *Salinospora* isolates appeared on a low nutrient medium (M4) indicating the importance of using appropriate isolation techniques. Thirteen representatives of eight different colony morphotypes were partially sequenced and the most phylogenetically diverse isolate (CNH898) was sequenced nearly in its entirety (GenBank Accession number AY040622) (SEQ ID NO:5).

Please replace paragraph [0029] with the following amended paragraph:

[0029] An examination of 30 actinomycetes with *Salinospora* morphological characteristics that were isolated from the Bahamas in 1989 (Jensen et al, 1991) revealed that all but two of these strains had an obligate requirement of seawater (Na^+) for growth. Ten seawater requiring strains representing six different morphotypes were partially sequenced and found to possess the five *Salinospora* signature nucleotides between positions 207- 468 (Table 3). The nearly complete 16S rDNA sequence of two of these (CNB440 and CNB536, Gen Bank Accession numbers AY040617 (SEQ ID NO:6) and AY040618 (SEQ ID NO:7), respectively) indicates that they are diverse members of the *Salinospora* clade (Figure 2). Thus, strains belonging to this new taxon have been isolated from near-shore Bahamian sediments on three separate occasions over an 11-year period indicating that they are persistent members of the sediment bacterial community.

Please replace paragraph [0030] with the following amended paragraph:

[0030] The two strains that did not require seawater for growth (CNB394 and CNB512) but had colony morphologies similar to *Salinospora* were found to lack the *Salinospora* signatures in Table 3. Analyses of the almost complete 16S rDNA sequence of these strains showed 99.6-99.9% similarity to *Micromonospora aurantiaca* str. W2b and the presence of all of the signature nucleotides previously published for the genus *Micromonospora* (Koch et al, 1996). The phylogenetic dendogram clearly shows that CNB394 and CNB512 are members of the genus *Micromonospora* (~~Figure 3~~ Figure 2). *Micromonospora* isolates have been reported from marine sediments (Takizawa et al, 1993), including deep-sea samples (Weyland, 1981), however, unlike *Salinospora,* this genus is well known from terrestrial soils and seawater-requiring strains have not been reported.

Please replace paragraph [0032] with the following amended paragraph:

[0032] To determine if *Salinospora* members had a broader distribution, sediments were collected from the Red Sea and the Sea of Cortez. From 42 Red Sea sediment samples, 22 isolates with *Salinospora* morphologies and an obligate requirement of seawater for growth were obtained. Six isolates representing 4 major morphotypes were partially sequenced and the almost complete 16S rDNA sequence of one strain (CNH725, GenBank Accession number AY040621) (SEQ ID NO:8) is represented in Figure 3. From 36 sediments collected in the Sea of Cortez, 20 seawater-requiring actinomycete strains were isolated and all of these possessed *Salinospora* morphological characteristics. Eight strains representing five different morphotypes were partially sequenced and the phylogenetically diverse isolate CNH964 (GenBank Accession number ~~AY040632~~ AY040623) was sequenced almost in its entirety ~~(Figure 3)~~. These results clearly indicate that *Salinospora* members are widely distributed in marine sediments.

Please replace paragraph [0033] with the following amended paragraph:

[0033] Phylogenetic analyses and physiological characteristics indicate that the *Salinospora* clade represents a new genus within the family Micromonosporaceae. Although it is unlikely

that the diversity within this genus has been revealed in the present study, intra-group 16S rDNA sequence similarity (98.6%) and a robust clade topology indicate that this genus is comprised of multiple species ~~(Figure 3)~~ (Figure 2). Placement of the genus *Salinospora* within the family Micromonosporaceae is supported by the presence of a complete set of family-specific 16S rDNA signature nucleotides (Stackelbrandt, 1997).

Please replace paragraph [0037] with the following amended paragraph:

[0037] *DNA purification, amplification, sequencing and phylogenetic analyses.* Genomic DNA was prepared as follows: 10 mg of vegetative mycelia grown on M1 agar for 2-4 weeks at 25-28°C was macerated and an aqueous cleared lysate, created by standard methods, was precipitated with 0.7 volumes of isopropanol. The resultant DNA pellet was then washed with 70% ethanol and resuspended in 10 mM Tris buffer (pH 8.5) to a final concentration of 100 ng/ml. 16S rDNA sequencing templates were amplified from 10-50 ng of genomic DNA template by the PCR using the primers FC27 (5' AGAGTTTGATCCTGGCTCAG) (SEQ ID 1) and RC1492 (5' TACGGCTACCTTGTTACGACTT) (SEQ ID 2). PCR products were purified with a Qiagen QlAquick PCR clean-up kit using the manufacture's protocols. Partial sequences of morphologically diverse strains were obtained from nucleotides 80-480 *(E. coli* numbering system) using the FC27 primer. Select 16S rDNA amplicons were sequenced almost in their entirety on both top and bottom strands using a total of ten primers. The ten contigs were then assembled yielding gene sequences of 1479 to 1483 unambiguous nucleotides. Hypervariable regions in the 16S rDNA sequences were excluded yielding a total of 1408 aligned nucleotides. 16S rDNA similarity values were calculated by the RDP similarity matrix online analysis and compared to the three nearest neighbors in the RDP database. Sequences were aligned to the secondary structure of members of the Micromonosporaceae in the RDP (Maidak et al, 2001) using the BioEdit software (Hall, 1999). Phylogenetic analyses were performed using the neighbor-joining and parsimony based algorithms in the Clustal W software and PHYLIP software packages, respectively (Thompson et al., 1994; Felsenstein, 1993). The dendogram ~~(Figure 3)~~ (Figure 2) was drawn using Treeview 1.6.1 (Page, 1996).